FILE 'EMBASE' ENTERED AT 13:03:05 ON 02 MAY 2005
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FILE 'BIOSIS' ENTERED AT 13:03:05 ON 02 MAY 2005
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FILE 'SCISEARCH' ENTERED AT 13:03:05 ON 02 MAY 2005
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FILE 'MEDLINE' ENTERED AT 13:03:05 ON 02 MAY 2005

=> s mmp (w) 12 or (macrophage elastase) or metalloelastase
L2 1380 MMP (W) 12 OR (MACROPHAGE ELASTASE) OR METALLOELASTASE

=> s antisense or oligonucleotide
L3 252733 ANTISENSE OR OLIGONUCLEOTIDE

=> s l2 and l3
L4 27 L2 AND L3

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 17 DUP REM L4 (10 DUPLICATES REMOVED)

=> d 1-17 l5 iall

L5 ANSWER 1 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 1
ACCESSION NUMBER: 2004330402 EMBASE
TITLE: Colony-stimulating factor-1 blockade by **antisense oligonucleotides** and small interfering RNAs suppresses growth of human mammary tumor xenografts in mice.
AUTHOR: Aharinejad S.; Paulus P.; Sioud M.; Hofmann M.; Zins K.; Schafer R.; Stanley E.R.; Abraham D.
CORPORATE SOURCE: S. Aharinejad, Lab. for Cardiovascular Research, Dept. of Anatomy and Cell Biology, Vienna Medical University, Waehringerstrasse 13, A-1090 Vienna, Austria. seyedhossein.aharinejad@meduniwien.ac.at
SOURCE: Cancer Research, (1 Aug 2004) Vol. 64, No. 15, pp. 5378-5384.
Refs: 47
ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040826
Last Updated on STN: 20040826
ABSTRACT: Colony-stimulating factor (CSF)-1 is the primary regulator of tissue macrophage production. CSF-1 expression is correlated with poor prognosis in breast cancer and is believed to enhance mammary tumor progression and metastasis through the recruitment and regulation of tumor-associated macrophages. Macrophages produce matrix metalloproteases (MMPs) and vascular endothelial growth factor, which are crucial for tumor invasion and angiogenesis. Given the important role of CSF-1, we hypothesized that blockade of CSF-1 or the CSF-1 receptor (the product of the c-fms proto-oncogene) would suppress macrophage infiltration and mammary tumor growth. Human MCF-7 mammary carcinoma cell xenografts in mice were treated with either mouse CSF-1 ***antisense*** **oligonucleotide** for 2 weeks or five intratumoral

injections of either CSF-1 small interfering RNAs or c-fms small interfering RNAs. These treatments suppressed mammary tumor growth by 50%, 45%, and 40%, respectively, and selectively down-regulated target protein expression in tumor lysates. Host macrophage infiltration; host **MMP-12**, MMP-2, and vascular endothelial growth factor A expression; and endothelial cell proliferation within tumors of treated mice were decreased compared with tumors in control mice. In addition, mouse survival significantly increased after CSF-1 blockade. These studies demonstrate that CSF-1 and CSF-1 receptor are potential therapeutic targets for the treatment of mammary cancer.

CONTROLLED TERM: Medical Descriptors:
*breast tumor: ET, etiology
*tumor xenograft
*cancer inhibition
macrophage
prognosis
tumor growth
metastasis
tumor associated leukocyte
receptor blocking
cancer invasion: ET, etiology
tumor vascularization: ET, etiology
angiogenesis
tumor angiogenesis
proto oncogene
proto oncogene c fms
cell infiltration
macrophage infiltration
protein expression
cell lysate
tumor lysate
endothelium cell
cell proliferation
survival
human
nonhuman
female
mouse
animal model
controlled study
human cell
animal tissue
animal cell
adolescent
article
priority journal
Drug Descriptors:
*colony stimulating factor 1
***antisense oligodeoxynucleotide**
*small interfering RNA
colony stimulating factor receptor
colony stimulating factor 1 receptor
matrix metalloproteinase
vasculotropin
gene product
macrophage elastase
gelatinase A
vasculotropin A
unclassified drug

CAS REGISTRY NO.: (colony stimulating factor 1) 81627-83-0; (vasculotropin) 127464-60-2; (gelatinase A) 146480-35-5; (vasculotropin A) 489395-96-2

L5 ANSWER 2 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2004402386 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15307189
TITLE: Reduced intragraft mRNA expression of matrix metalloproteinases Mmp3, Mmp12, Mmp13 and Adam8, and diminished transplant arteriosclerosis in Ccr5-deficient mice.
AUTHOR: Luckow Bruno; Joergensen Joanne; Chilla Silvia; Li Jian-Ping; Henger Anna; Kiss Eva; Wieczorek Grazyna; Roth Lukas; Hartmann Nicole; Hoffmann Reinhard; Kretzler Matthias; Nelson Peter J; Perez de Lema Guillermo; Maier Holger; Wurst Wolfgang; Balling Rudi; Pfeffer Klaus; Grone Hermann-Josef; Schlondorff Detlef; Zerwes Hans-Gunter
CORPORATE SOURCE: Klinikum der Universitat Munchen, Medizinische Poliklinik--Innenstadt, Munchen, Germany.. bruno.luckow@med.uni-muenchen.de
SOURCE: European journal of immunology, (2004 Sep) 34 (9) 2568-78. Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 20040813
Last Updated on STN: 20041008
Entered Medline: 20041007
ABSTRACT:
Experimental and human organ transplant studies suggest an important role for chemokine (C-C-motif) receptor-5 (CCR5) in the development of acute and chronic allograft rejection. Because early transplant damage can predispose allografts to chronic dysfunction, we sought to identify potential pathophysiologic mechanisms leading to allograft damage by using wild-type and Ccr5-deficient mice as recipients of fully MHC-mismatched heart and carotid-artery allografts. Gene expression in rejecting heart allografts was analyzed 2 and 6 days after transplantation using Affymetrix GeneChips. Microarray analysis led to identification of four metalloproteinase genes [matrix metalloproteinase (Mmp)3, Mmp12, Mmp13 and a disintegrin and metalloprotease domain (Adam)8] with significantly diminished intragraft mRNA expression in Ccr5-deficient mice at day 6. Accordingly, allografts from Ccr5-deficient mice showed less tissue remodeling and hence better preservation of the myocardial architecture compared with allografts from wild-type recipients. Moreover, survival of cardiac allografts was significantly increased in Ccr5-deficient mice. Carotid artery allografts from Ccr5-deficient recipients showed better tissue preservation, and significant reduction of neointima formation and CD3+ T cell infiltration. Ccr5 appears to play an important role in transplant-associated arteriosclerosis that may involve metalloproteinase-mediated vessel wall remodeling. We conclude that early tissue remodeling may be a critical feature in the predisposition of allografts to the development of chronic dysfunction.

CONTROLLED TERM: Animals
*Antigens, CD: GE, genetics
*Arteriosclerosis: PC, prevention & control
Carotid Arteries: TR, transplantation
*Collagenases: GE, genetics
Cyclosporine: PD, pharmacology
*Heart Transplantation: AE, adverse effects
*Membrane Proteins: GE, genetics
*Metalloendopeptidases: GE, genetics
Mice
Mice, Inbred BALB C
Mice, Inbred C57BL
***Oligonucleotide Array Sequence Analysis**
*RNA, Messenger: AN, analysis

*Receptors, CCR5: PH, physiology
Research Support, Non-U.S. Gov't
*Stromelysin 1: GE, genetics
Transplantation, Homologous
CAS REGISTRY NO.: 59865-13-3 (Cyclosporine)
CHEMICAL NAME: 0 (Antigens, CD); 0 (Membrane Proteins); 0 (RNA, Messenger); 0 (Receptors, CCR5); EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.- (Adam8 protein, mouse); EC 3.4.24.- (Collagenases); EC 3.4.24.- (alveolar **macrophage elastase**); EC 3.4.24.- (collagenase 3); EC 3.4.24.17 (Stromelysin 1)

L5 ANSWER 3 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2004037774 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14647437
TITLE: MMP expression profiling in recurred stage IB lung cancer.
AUTHOR: Cho Nam Hoon; Hong Kyi Pyo; Hong Sung Hui; Kang Suki; Chung Kyung Young; Cho Sang Ho
CORPORATE SOURCE: Department of Pathology, Yonsei University College of Medicine, Seoul, Korea.
SOURCE: Oncogene, (2004 Jan 22) 23 (3) 845-51.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20040123
Last Updated on STN: 20040304
Entered Medline: 20040303

ABSTRACT:
We aimed to clarify the prime role of recurrence in stage I lung cancer. To determine the expression profiles, quantitative RT-PCR and real-time PCR were performed subsequently to evaluate the validity of meaningful molecules identified by 0.12 K c-DNA array experiment surveys. In all, 10 lung cancer patients presenting with recurrence of stage IB were selected and compared with 10 stage IB lung cancer patients without recurrence since biopsied 3 years previously. On c-DNA microarray data analysis using pairs of recurred and the corresponding nonrecurred patients, the following genes were found to be upregulated in the recurred cases: matrix metalloproteinase (MMP)-10 in five cases, **MMP-12** in two cases, MMP-11, MMP-14, MMP-15, fos, cyclin E2, E2F3, TGF-alpha in each one case. The most frequently upregulated genes in recurred lung cancers were MMP-10 (stromelysin-2) and **MMP-**
12 (**macrophage elastase**). On transcriptional assay by quantitative RT-PCR and real-time RT-PCR analysis to validate those molecules, both transcripts of MMP-10 and **MMP-12** were significantly more upregulated in recurred stage IB lung cancer than in the non-recurred stage IB lung cancer (P=0.004). Transcript levels were identical to c-DNA array data. The protein levels of these entities were also evaluated by immunohistochemistry of archival slides. By immunohistochemistry, MMP-10 monoclonal antibody showed more intense immunoreactivity in the recurred stage IB lung cancer than in the nonrecurred stage IB lung cancer (P=0.0313). Our approach revealed that MMP-10 plays an important role in the recurrence in stage IB lung cancer, irrespective of the histologic type.

CONTROLLED TERM: Base Sequence
Carcinoma, Non-Small-Cell Lung: EN, enzymology
*Carcinoma, Non-Small-Cell Lung: GE, genetics
DNA Primers
*Gene Expression Profiling
Humans
Immunohistochemistry
Lung Neoplasms: EN, enzymology
*Lung Neoplasms: GE, genetics

*Matrix Metalloproteinases: GE, genetics
Oligonucleotide Array Sequence Analysis
Recurrence
Research Support, Non-U.S. Gov't
Reverse Transcriptase Polymerase Chain Reaction
Transcription, Genetic

CHEMICAL NAME: 0 (DNA Primers); EC 3.4.24.- (Matrix Metalloproteinases)

L5 ANSWER 4 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2004113115 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14644759
TITLE: Lysosomal acid lipase deficiency causes respiratory inflammation and destruction in the lung.
AUTHOR: Lian Xuemei; Yan Cong; Yang Li; Xu Yan; Du Hong
CORPORATE SOURCE: Div. of Human Genetics, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave., Cincinnati, OH 45229-3039, USA.
CONTRACT NUMBER: DK-54930 (NIDDK)
HL-061803 (NHLBI)
HL-067862 (NHLBI)
SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2004 Apr) 286 (4) L801-7. Electronic Publication: 2003-11-26.
Journal code: 100901229. ISSN: 1040-0605.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20040309
Last Updated on STN: 20040427
Entered Medline: 20040426

ABSTRACT:
The functional roles of neutral lipids are poorly understood in the lung. Blocking cholesteryl ester and triglyceride metabolism in lysosomal acid lipase gene knockout mice (lal-/-) resulted in a high level of neutrophil influx in the lungs as early as 2 mo of age. Bronchoalveolar macrophages appeared foamy and gradually increased in number with age progression. Affymetrix GeneChip array analysis of lung mRNA showed increased levels of proinflammatory cytokine (including IL-1beta, IL-6, and TNF-alpha) and matrix metalloproteinase (including MMP-8, MMP-9, and **MMP-12**) expression in lal-/- mice. With age progression, some areas of lal-/- mice developed severe abnormal cell proliferation and alveolar remodeling. In other areas, alveolar destruction (i.e., emphysema) was observed. In addition, Clara cell hypertrophy and hyperplasia developed in conducting airways. The pathophysiological phenotypes in the lal-/- mouse lungs became more severe with increasing age. The studies support the concept that neutral lipid metabolites play essential roles in pulmonary homeostasis, inflammatory responses, remodeling, and injury repair.

CONTROLLED TERM: Animals
Chemokines: GE, genetics
Cytokines: GE, genetics
Emphysema: IM, immunology
*Emphysema: ME, metabolism
*Emphysema: PA, pathology
Hyperplasia
Hypertrophy
Lipase: DF, deficiency
*Lipase: GE, genetics
Lipids: ME, metabolism
Lysosomes: EN, enzymology
Macrophages, Alveolar: IM, immunology
Matrix Metalloproteinases: GE, genetics

Mice
Mice, Mutant Strains
Neutrophils: IM, immunology
Oligonucleotide Array Sequence Analysis
Phenotype
Pneumonia: IM, immunology
*Pneumonia: ME, metabolism
*Pneumonia: PA, pathology
Pulmonary Alveoli: IM, immunology
Pulmonary Alveoli: ME, metabolism
Pulmonary Alveoli: PA, pathology
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.

CHEMICAL NAME: 0 (Chemokines); 0 (Cytokines); 0 (Lipids); EC 3.1.1.3 (Lipase); EC 3.4.24.- (Matrix Metalloproteinases)

L5 ANSWER 5 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2003113667 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12626598
TITLE: Macrophage **metalloelastase** as a major factor for glomerular injury in anti-glomerular basement membrane nephritis.
AUTHOR: Kaneko Yoshikatsu; Sakatsume Minoru; Xie Yuansheng; Kuroda Takeshi; Igashima Michiko; Narita Ichiei; Gejyo Fumitake
CORPORATE SOURCE: Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences and Kidney Center, Shinraku-en Hospital, Niigata, Japan.. kanekoy@med.niigata-u.ac.jp
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2003 Mar 15) 170 (6) 3377-85.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030311
Last Updated on STN: 20030626
Entered Medline: 20030625

ABSTRACT:
Rat anti-glomerular basement membrane (GBM) nephritis is a model of crescentic glomerulonephritis induced by injection of anti-GBM antiserum. To elucidate the mechanism of glomerular injury, we analyzed the gene expression patterns in the kidneys of anti-GBM nephritis rats using DNA arrays, and found that macrophage **metalloelastase**/matrix metalloproteinase (**MMP**)-***12*** was one of the highly expressed genes in the kidneys on days 3 and 7 after the injection of anti-GBM antiserum. Enhancement of **MMP**-***12*** mRNA expression was confirmed by Northern blot analysis, and in situ hybridization revealed that **MMP-12** mRNA was expressed in ED-1-positive macrophages and multinuclear giant cells in the glomeruli with crescent. Moreover, these cells were positive with anti-rat rMMP-12 Ab on the section of the kidneys of anti-GBM nephritis rats on day 7. To clarify the role of **MMP-12**, we conducted a neutralization experiment using anti-rat rMMP-12 Ab, which had an ability to inhibit rMMP-12 activity of degrading natural substrate such as bovine elastin or human fibronectin in vitro. Anti-rat rMMP-12 Ab or control Ig was injected in each of six rats on days 0, 2, 4, and 6 after the injection of anti-GBM antiserum. Consequently, crescent formation and macrophage infiltration in the glomeruli were significantly reduced in the rats treated with anti-rat rMMP-12 Ab, and the amount of urine protein was also decreased. These results disclosed that ***MMP*** **-12** played an important role in glomerular injury in a crescentic glomerulonephritis model, and inhibition of **MMP-12** may lead to a new therapeutic strategy for this disease.

CONTROLLED TERM: Check Tags: Male
Animals
*Anti-Glomerular Basement Membrane Disease: EN, enzymology
Anti-Glomerular Basement Membrane Disease: IM, immunology
*Anti-Glomerular Basement Membrane Disease: PA, pathology
Anti-Glomerular Basement Membrane Disease: PC, prevention & control
Blotting, Northern
Blotting, Western
Cell Movement: IM, immunology
Gene Expression Regulation: IM, immunology
Immune Sera: AD, administration & dosage
In Situ Hybridization
Injections, Intravenous
*Kidney Glomerulus: EN, enzymology
*Kidney Glomerulus: PA, pathology
*Macrophages: EN, enzymology
*Metalloendopeptidases: AE, adverse effects
Metalloendopeptidases: BI, biosynthesis
Metalloendopeptidases: GE, genetics
Oligonucleotide Array Sequence Analysis
Rats
Rats, Inbred WKY
Recombinant Proteins: AD, administration & dosage
Recombinant Proteins: TU, therapeutic use
Research Support, Non-U.S. Gov't
Substrate Specificity

CHEMICAL NAME: 0 (Immune Sera); 0 (Recombinant Proteins); EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.- (alveolar **macrophage elastase**)

L5 ANSWER 6 OF 17 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:900605 SCISEARCH
THE GENUINE ARTICLE: 732KR
TITLE: Comparing genomic and histologic correlations to radiographic changes in tumors: A murine SCCVII model study
AUTHOR: Yang Y S; Guccione S; Bednarski M D (Reprint)
CORPORATE SOURCE: Stanford Univ, Sch Med, Dept Radiol, MRS Res Ctr, Stanford, CA 94305 USA (Reprint); NIH, Ctr Clin, Radiol & Imaging Sci Program, Bethesda, MD 20892 USA
COUNTRY OF AUTHOR: USA
SOURCE: ACADEMIC RADIOLOGY, (OCT 2003) Vol. 10, No. 10, pp. 1165-1175.
Publisher: ASSOC UNIV RADIOLOGISTS, 820 JORIE BLVD, OAK BROOK, IL 60523-2251 USA.
ISSN: 1076-6332.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 54
ABSTRACT:

Rationale and Objectives. To investigate the correlation between the temporal changes in T1- and T2-weighted contrast-enhanced magnetic resonance imaging (MRI), histologic evaluation, and genomic analysis using ***oligonucleotide*** microarrays in a murine squamous cell carcinoma tumor models.

Materials and Methods. The squamous cell carcinoma (SCC VII) cell line was used to initiate subcutaneous tumors in mice. This mouse model has been used as a model for human head and neck carcinomas. Animals were imaged using contrast enhanced MRI (CE-MRI). Different stages of tumor growth were defined based on changes in the T1- and T2-weighted MRI patterns. The contrast enhancing (CE) and nonenhancing (NE) regions of the tumors were marked and biopsied for

oligonucleotide microarray and histologic analysis. Tumors with no differential contrast enhancement were used as controls.

Results. Distinct temporal stages of tumor progression can be defined using both T1- and T2-weighted CE-MRI and microarray analysis. The early stage tumors show a homogeneous contrast enhancement pattern in the T1- and T2-weighted images with no significant differential gene expression from the center and periphery of the tumor. The more advanced tumors that show discrete regions of contrast enhancement in the post-contrast T1-weighted MRIs and tissues from the CE and NE regions show distinctly differential gene expression profiles. Histologic analysis (hematoxylin-eosin stain) showed that the samples obtained from the periphery and center of the early stage tumors and the CE and NE regions from these more advanced tumors were similar. The gene expression profiles of late-stage tumors that showed changes in T2-weighted MRI signal intensity were consistent with tissue degradation in the NE region, which also showed characteristic signs of tissue necrosis in histologic analysis.

Conclusion. These results show that temporal changes in T1- and T2-weighted CE-MRI are related to distinct gene expression profiles, and histologic analysis may not be sufficient to detect these detailed changes. As tumors progress, discrete regions of post-contrast T1 enhancement are identified; these regions have distinct gene expression patterns despite similar histologic features. In late-stage tumors, regions of T2 signal changes are observed which correspond with tissue necrosis.

CATEGORY: RADIOLOGY, NUCLEAR MEDICINE & MEDICAL IMAGING
SUPPLEMENTARY TERM: contrast-enhanced magnetic resonance imaging (MRI); functional genomics; microarray analysis; animal tumor model; histologic analysis
SUPPL. TERM PLUS: ENDOTHELIAL GROWTH-FACTOR; SQUAMOUS-CELL CARCINOMA; ANGIOGENESIS IN-VITRO; GENE-EXPRESSION; MACROPHAGE **METALLOELASTASE**; MOLECULAR CLASSIFICATION; EXTRACELLULAR-MATRIX; MAGNETIC-RESONANCE; CANCER; INTERLEUKIN-1

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ALEXANDER J	2003			P 89 ANN M RAD SOC N
ALIZADEH A A	2000	403	503	NATURE
ANDERSON G R	2001	81	501	CURR SCI INDIA
BATTEGAY E J	1994	125	917	J CELL BIOL
BITTNER M	2000	406	536	NATURE
BORK P	1993	327	125	FEBS LETT
BOSTROM P J	2000	88	417	INT J CANCER
BRASCH R	1997	7	68	JMRI-J MAGN RESON IM
CLARK E A	2000	406	532	NATURE
COCHRAN A J	2000	30	11	SEMIN NUCL MED
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DINARELLO C A	2000	343	732	NEW ENGL J MED
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FERRARA N	1999	5	1359	NAT MED
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GILLIES R J	2000	2	139	NEOPLASIA
GOLUB T R	1999	286	531	SCIENCE
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GOURDON G	1995	86	766	BLOOD
GRIMBERG A	2000	183	1	J CELL PHYSIOL
GUCCIONE S	2003	228	560	RADIOLOGY
GUCCIONE S	2002			P 88 ANN M RAD SOC N
GUCCIONE S	2003			P ANN M AM SOC CLIN
HELDIN C H	1999	79	1283	PHYSIOL REV

HOMER J J	2000	25	169	CLIN OTOLARYNGOL
JOHANSSON N	2000	57	5	CELL MOL LIFE SCI
KAO C M	1999	15	304	BIOTECHNOL PROGR
KIM S	2000	252	173	GENE
KIM J E	2000	77	169	J CELL BIOCHEM
MASHIMA T	2001	188	352	J CELL PHYSIOL
MCKINNON P J	2000	20	656	MOL CELL BIOL
MIANO J M	2000	87	355	CIRC RES
MIETTINEN M	1999	22	219	J HISTOTECHNOL
NAKAJIMA M	2002	178	99	CANCER LETT
NEEMAN M	2001	11	70	SEMIN RADIAT ONCOL
NICOSIA R F	1994	145	1023	AM J PATHOL
NING S C	1999	50	215	RADIOTHER ONCOL
PEROU C M	1999	96	9212	P NATL ACAD SCI USA
PEROU C M	2000	406	747	NATURE
PHAM C	1992	16	225	CANC INVEST
PUPA S M	2002	192	259	J CELL PHYSIOL
RICKWELL S	2001		133	TUMOUR MICROENVIRONM
RUOSLAHTI E	1999	76	1	ADV CANCER RES
SCHERF U	2000	24	236	NAT GENET
TAE K	2000	6	2821	CLIN CANCER RES
TRIMBOM T	1998	13	112	GENE DEV
VANDERREST M	1991	5	2814	FASEB J
VOGEL T	1994	18	274	J CELL BIOCHEM
WESTERMARCK J	1999	13	781	FASEB J
WU T D	2001	195	53	J PATHOL
ZIEMER L S	2001	3	500	NEOPLASIA

L5 ANSWER 7 OF 17 MEDLINE on STN

ACCESSION NUMBER: 2003434368 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12963695

TITLE: Matrilysin-dependent elastolysis by human macrophages.

AUTHOR: Filippov Sergey; Caras Ingrid; Murray Richard; Matrisian Lynn M; Chapman Harold A Jr; Shapiro Steven; Weiss Stephen J

CORPORATE SOURCE: University of Michigan Comprehensive Cancer Center, Ann Arbor, MI 48109, USA.

CONTRACT NUMBER: AI21301 (NIAID)

SOURCE: Journal of experimental medicine, (2003 Sep 15) 198 (6) 925-35. Electronic Publication: 2003-09-08.
Journal code: 2985109R. ISSN: 0022-1007.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200311

ENTRY DATE: Entered STN: 20030917
Last Updated on STN: 20031108
Entered Medline: 20031107

ABSTRACT:
Human macrophages found in juxtaposition to fragmented elastin in vivo express the elastolytic matrix metalloproteinases (MMPs) progelatinase B, prometalloelastase, and promatrilysin. Though MMPs can degrade a range of extracellular matrix components, increasing evidence suggests that preferred targets in vivo include nonmatrix substrates such as chemokines and growth factors. Hence, the means by which MMPs participate in elastin turnover remain undefined as does the identity of the elastolysins. Herein, human macrophage cultures have been established that express a complement of elastolytic proteinases similar, if not identical, to that found in vivo. Under plasminogen-free conditions, macrophages preferentially use ***metalloelastase*** to mediate elastolysis via a process that deposits active enzyme on elastin surfaces. By contrast, in the presence of plasminogen, human macrophages up-regulate proteolysis 10-fold by processing

promatrilysin to an active elastolysin via a urokinase-type plasminogen activator-dependent pathway. Matrilysin-deficient human macrophages fail to mediate an elastolytic response despite the continued expression of gelatinase B and **metalloelastase**. Thus, acting in concert with cosecreted cysteine proteinases whose activities are constrained to sites of macrophage-elastin contact (Punturieri, A., S. Filippov, E. Allen, I. Caras, R. Murray, V. Reddy, and S.J. Weiss. 2000. J. Exp. Med. 192:789-799), matrilysin confers macrophages with their most potent MMP-dependent elastolytic system.

CONTROLLED TERM:
Animals
Aorta: CY, cytology
Aorta: ME, metabolism
Cathepsins: ME, metabolism
Cells, Cultured
Culture Media, Conditioned
Culture Media, Serum-Free
*Elastin: ME, metabolism
Enzyme Inhibitors: ME, metabolism
Gelatinase B: ME, metabolism
Humans
Macrophages: CY, cytology
*Macrophages: ME, metabolism
Matrilysin: GE, genetics
*Matrilysin: ME, metabolism
Oligonucleotide Array Sequence Analysis
Pancreatic Elastase: GE, genetics
Pancreatic Elastase: ME, metabolism
Plasminogen: ME, metabolism
Plasminogen Activators: ME, metabolism
Research Support, U.S. Gov't, P.H.S.

CAS REGISTRY NO.: 9001-91-6 (Plasminogen); 9007-58-3 (Elastin)

CHEMICAL NAME: 0 (Culture Media, Conditioned); 0 (Culture Media, Serum-Free); 0 (Enzyme Inhibitors); EC 3.4.- (Cathepsins); EC 3.4.21.- (Plasminogen Activators); EC 3.4.21.36 (Pancreatic Elastase); EC 3.4.24.23 (Matrilysin); EC 3.4.24.35 (Gelatinase B)

L5 ANSWER 8 OF 17 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 2

ACCESSION NUMBER: 2003:500435 SCISEARCH

THE GENUINE ARTICLE: 687BG

TITLE: Ozone-induced disruptions of lung transcriptomes

AUTHOR: Gohil K (Reprint); Cross C E; Last J A

CORPORATE SOURCE: Univ Calif Davis, Ctr Comparat Resp & Med, Dept Internal Med, Davis, CA 95616 USA (Reprint)

COUNTRY OF AUTHOR: USA

SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (6 JUN 2003) Vol. 305, No. 3, pp. 719-728.
Publisher: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
ISSN: 0006-291X.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 60

ABSTRACT:

We have analyzed changes in similar to4000 lung mRNAs, with GeneChips, in mice exposed to I ppm O-3 for three consecutive nights (8 h per night). Differential gene expression analysis identified similar to260 O-3 sensitive genes; similar to80% of these were repressed and similar to20% were induced in O-3-exposed mice compared to the air-exposed controls. A 20-fold induction of serum amyloid A3 mRNA by O-3 suggested activation of NF-kappaB and CCAAT/enhancer binding protein-mediated pathways by inflammatory cytokines. Induction (up to 14-fold) of 12 genes that increase DNA synthesis and cell

cycle progression, and increase (similar to7-fold) in CD44 mRNA and macrophage ***metalloelastase*** suggested a state Of O-3-induced hyperplasia and lung remodeling. Several mRNAs encoding enzymes of xenobiotic metabolism and cytoskeletal functions were repressed and may suggest cytokine mediated suppression of cytochrome P450 expression and cachexia-like inflammatory state in ozone-exposed lungs. The expressions of similar to30 genes of immune response were also repressed. Collectively this genome-wide analysis of lungs identified ozone-induced disruption of gene transcriptional profile indicative of increased cellular proliferation under suppressed immune surveillance and xenobiotic metabolism.

CATEGORY: BIOCHEMISTRY & MOLECULAR BIOLOGY; BIOPHYSICS
SUPPLEMENTARY TERM: cell cycle; transcription factors; cachexia; MHC; immune response; **oligonucleotide** arrays
SUPPL. TERM PLUS: NF-KAPPA-B; TUMOR-NECROSIS-FACTOR; CYCLE-DEPENDENT REGULATION; CELL-CYCLE; RIBONUCLEOTIDE REDUCTASE; EPITHELIAL PROLIFERATION; **OLIGONUCLEOTIDE** ARRAYS; GENE-EXPRESSION; END-PRODUCTS; RAT LUNGS

REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
ADACHI N	1997	230	105	BIOCHEM BIOPH RES CO
ARGILES J M	1999	19	223	MED RES REV
BAUD V	2001	11	372	TRENDS CELL BIOL
BING Z Y	2000	275	31616	J BIOL CHEM
CAI L	1999	132	85	TOXICOLOGY
CHANG H R	1998	22	156	JPEN-PARENTER ENTER
CHENG P Y	2001	2	165	CURR DRUG METAB
CHO H Y	2001	280	L537	AM J PHYSIOL-LUNG C
COHEN M D	2001	171	71	TOXICOL APPL PHARM
CRACOWSKI J L	2001	38	93	J VASC RES
DERISI J L	1997	278	680	SCIENCE
DUDEK S M	2001	91	1487	J APPL PHYSIOL
ELLEDGE S J	1990	4	740	GENE DEV
ELSAYED N M	1990	102	1	TOXICOL APPL PHARM
ERIKSSON S	1984	259	11695	J BIOL CHEM
FAKHRZADEH L	2002	26	413	AM J RESP CELL MOL
GELLERT M	2002	71	101	ANNU REV BIOCHEM
GELZLEICHTER T R	1992	112	73	TOXICOL APPL PHARM
GOHIL K	2000	33	831	FREE RADICAL RES
GOLDSTEIN B D	1978		295	CIBA FOUND S
GUTTRIDGE D C	2000	289	2363	SCIENCE
HIROSHIMA K	1987	47	327	EXP MOL PATHOL
HUMPHREYS D	1997	36	15233	BIOCHEMISTRY-US
JAGOE R T	2002	16	1697	FASEB J
JAMALUDDIN M	2001	280	L248	AM J PHYSIOL-LUNG C
JANG A S	2002	57	737	ALLERGY
KAMINSKI N	2000	97	1778	P NATL ACAD SCI USA
KATSUOKA F	1997	238	512	BIOCHEM BIOPH RES CO
KENYON N J	2002	282	L540	AM J PHYSIOL-LUNG C
KLEEBERGER S R	2001	90	713	J APPL PHYSIOL
KOPP E B	1999	11	13	CURR OPIN IMMUNOL
LASKIN D L	2002	234	91	MOL CELL BIOCHEM
LEE E G	2000	289	2350	SCIENCE
LEFFERS H	1993	231	982	J MOL BIOL
LEIKAUF G D	2001			558 RS REP HLTH EFF
LERCHGAGGL A	2002	277	45347	J BIOL CHEM
LI Q T	2002	2	725	NAT REV IMMUNOL
LIEBERAM I	1999	29	2684	EUR J IMMUNOL
LIPSHUTZ R J	1999	21	20	NAT GENET S
LISTON P	1996	379	349	NATURE
LOCKHART D J	1996	14	1675	NAT BIOTECHNOL

LONGPHRE M	1999	86	341	J APPL PHYSIOL
MANGO G W	1998	275	L348	AM J PHYSIOL-LUNG C
NEEPER M	1992	267	14998	J BIOL CHEM
OKITA R T	1996	31	101	CRIT REV BIOCHEM MOL
PRYOR W A	1991	4	341	CHEM RES TOXICOL
PUNJABI C J	1994	11	165	AM J RESP CELL MOL B
RUAN H	2002	51	1319	DIABETES
SCHUSTER J M	2000	67	767	J LEUKOCYTE BIOL
SHASTRI N	2002	20	463	ANNU REV IMMUNOL
SINGAL D P	1996	68	629	INT J CANCER
TIAN B	2002	76	6800	J VIROL
UMBRICHT C B	2001	20	3348	ONCOGENE
VANESS P J	2002	300	824	J PHARMACOL EXP THER
WARD P P	2002	80	95	BIOCHEM CELL BIOL
WATANABE C M H	2001	98	6577	P NATL ACAD SCI USA
WODICKA L	1997	15	1359	NAT BIOTECHNOL
WU L	1991	174	1617	J EXP MED
YARMUSH M L	2002	4	349	ANNU REV BIOMED ENG
ZHAO Q Y	1998	274	L39	AM J PHYSIOL-LUNG C

L5 ANSWER 9 OF 17 EMBASE
on STN

ACCESSION NUMBER: 2003216876 EMBASE

TITLE: PTP1B **antisense**-treated mice show regulation of genes involved in lipogenesis in liver and fat.

AUTHOR: Waring J.F.; Ciurlionis R.; Clampit J.E.; Morgan S.; Gum R.J.; Jolly R.A.; Kroeger P.; Frost L.; Trevillyan J.; Zinker B.A.; Jirousek M.; Ulrich R.G.; Rondinone C.M.

CORPORATE SOURCE: J.F. Waring, Dept. of Cell./Molecular Toxicology, Abbott Laboratories R463, Abbott Park, IL 60064-6104, United States. jeff.waring@abbott.com

SOURCE: Molecular and Cellular Endocrinology, (30 May 2003) Vol. 203, No. 1-2, pp. 155-168.
Refs: 41
ISSN: 0303-7207 CODEN: MCEND6

COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
022 Human Genetics
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20030619
Last Updated on STN: 20030619

ABSTRACT: Protein tyrosine phosphatases are important regulators of insulin signal transduction. Our studies have shown that in insulin resistant and diabetic ob/ob and db/db mice, reducing the levels of protein tyrosine phosphatase 1B (PTP1B) protein by treatment with a PTP1B **antisense** ***oligonucleotide*** resulted in improved insulin sensitivity and normalized plasma glucose levels. The mechanism by which PTP1B inhibition improves insulin sensitivity is not fully understood. We have used microarray analysis to compare gene expression changes in adipose tissue, liver and muscle of PTP1B ***antisense*** -treated ob/ob mice. Our results show that treatment with PTP1B **antisense** resulted in the downregulation of genes involved in lipogenesis in both fat and liver, and a downregulation of genes involved in adipocyte differentiation in fat, suggesting that PTP1B **antisense** acts through a different mechanism than thiazolidinedione (TZD) treatment. In summary, microarray results suggest that reduction of PTP1B may alleviate hyperglycemia and enhance insulin sensitivity by a different mechanism than TZD treatment.

CONTROLLED TERM:

Medical Descriptors:
*lipogenesis
*gene expression regulation
*diabetes mellitus: ET, etiology
*insulin resistance: ET, etiology
insulin sensitivity
glucose blood level
DNA microarray
adipose tissue
liver
muscle tissue
down regulation
adipocyte
cell differentiation
nucleic acid analysis
drug effect
gene control
histopathology
nonhuman
mouse
animal experiment
animal model
controlled study
animal tissue
article
nucleotide sequence
priority journal
Drug Descriptors:
*protein tyrosine phosphatase: EC, endogenous compound
***antisense oligonucleotide: CM, drug comparison**
***antisense oligonucleotide: PD, pharmacology**
***antisense oligonucleotide: IP, intraperitoneal drug administration**
glucose: EC, endogenous compound
thiazolidine derivative: CM, drug comparison
thiazolidine derivative: PD, pharmacology
thiazolidine derivative: IP, intraperitoneal drug administration
protein inhibitor: CM, drug comparison
protein inhibitor: PD, pharmacology
protein inhibitor: IP, intraperitoneal drug administration
rosiglitazone: CM, drug comparison
rosiglitazone: PD, pharmacology
rosiglitazone: IP, intraperitoneal drug administration
protein kinase: EC, endogenous compound
vimentin: EC, endogenous compound
entactin: EC, endogenous compound
interferon regulatory factor 7: EC, endogenous compound
macrophage elastase: EC, endogenous compound
transcription factor: EC, endogenous compound
adenylate kinase: EC, endogenous compound
cytokeratin: EC, endogenous compound
oncoprotein: EC, endogenous compound
lymphocyte antigen: EC, endogenous compound
fructose bisphosphatase: EC, endogenous compound
malate dehydrogenase (decarboxylating): EC, endogenous compound
adenosine triphosphate citrate lyase: EC, endogenous compound
cytochrome P450: EC, endogenous compound
somatomedin: EC, endogenous compound
oxygenase: EC, endogenous compound
scatter factor: EC, endogenous compound

glucose transporter: EC, endogenous compound
liver protein: EC, endogenous compound
membrane protein: EC, endogenous compound
thyroid hormone receptor: EC, endogenous compound
cathepsin D: EC, endogenous compound
CD72 antigen: EC, endogenous compound
unindexed drug
isis 113715

CAS REGISTRY NO.: (protein tyrosine phosphatase) 79747-53-8, 97162-86-2; (glucose) 50-99-7, 84778-64-3; (rosiglitazone) 122320-73-4, 155141-29-0; (protein kinase) 9026-43-1; (adenylate kinase) 9013-02-9; (fructose bisphosphatase) 9001-52-9; (malate dehydrogenase (decarboxylating)) 9028-46-0, 9074-02-6, 9080-52-8; (adenosine triphosphate citrate lyase) 9027-95-6; (cytochrome P450) 9035-51-2; (oxygenase) 9037-29-0, 9046-59-7; (scatter factor) 67256-21-7, 72980-71-3; (cathepsin D) 9025-26-7

CHEMICAL NAME: Isis 113715

GENE NUMBER: GENBANK I38444 referred number; GENBANK L32973 referred number; GENBANK M11686 referred number; GENBANK M18184 referred number; GENBANK M33863 referred number; GENBANK M55637 referred number; GENBANK M73696 referred number; GENBANK M82831 referred number; GENBANK U04827 referred number; GENBANK U25844 referred number; GENBANK U41341 referred number; GENBANK U43084 referred number; GENBANK U73037 referred number; GENBANK X14194 referred number; GENBANK X51438 referred number; GENBANK X54542 referred number; GENBANK X91824 referred number

L5 ANSWER 10 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 3

ACCESSION NUMBER: 2003274166 EMBASE

TITLE: Distinct gene expression of osteopontin in patients with ulcerative colitis.

AUTHOR: Masuda H.; Takahashi Y.; Asai S.; Takayama T.

CORPORATE SOURCE: Dr. H. Masuda, Third Department of Surgery, Nihon University School of Medicine, 2-11-1, Hikarigaoka, Nerima-ku, Tokyo 179-0072, Japan. hidekim@med.nihon-u.ac.jp

SOURCE: Journal of Surgical Research, (1 May 2003) Vol. 111, No. 1, pp. 85-90.
Refs: 35
ISSN: 0022-4804 CODEN: JSGRA2

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
009 Surgery
022 Human Genetics
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20030724
Last Updated on STN: 20030724

ABSTRACT: Background. Ulcerative colitis (UC) is a multifactorial disorder of unknown etiology. Few studies have applied genome-wide gene expression analysis in colon tissue samples of UC. We report the analysis of mucosal gene expression in UC and noninflamed control specimens. Materials and methods. This study included 7 UC patients who received a total colectomy because of severe total colitis. Normal control colon tissues were obtained at least 10 cm from the area of pathology in 3 colon cancer patients. Ten colonic tissue samples (7 UC and 3 normal control samples) were subjected to high-density ***oligonucleotide*** array analysis. To compare differences in the level of gene expression between UC and control samples, Mann-Whitney U-test was used, with significance set at $P < 0.05$. Results. Twenty-five genes had a

3.0.apprx.23.4-fold higher mRNA expression in UC samples compared with normal samples, whereas three genes had a 3.0 .apprx. 3.4-fold lower expression in UC samples compared with normal samples. Two genes showing more than a 10-fold increase expression in UC samples were a macrophage **metalloelastase** (L23808) and a osteopontin (AF052124). It has been said that macrophage ***metalloelastase*** is related to ulcer formation of the intestine, whereas osteopontin plays an important role in the pathogenesis of systemic lupus erythematosus and rheumatoid arthritis. Conclusion. Our present study supports the previous report that macrophage **metalloelastase** is related to ulcer formation of UC, and it also indicates the possibility that osteopontin plays an important role in the pathogenesis of UC via increased immune activity.

CONTROLLED TERM: Medical Descriptors:
*ulcerative colitis: SU, surgery
gene expression
genetic analysis
colon mucosa
colon resection
disease severity
colon
colon cancer
cancer patient
sample
DNA microarray
rank sum test
ulcerogenesis
intestine ulcer
gene function
pathogenesis
systemic lupus erythematosus
rheumatoid arthritis
human
clinical article
controlled study
human tissue
adult
article
nucleotide sequence
priority journal
Drug Descriptors:
*osteopontin
messenger RNA
macrophage elastase
CAS REGISTRY NO.: (osteopontin) 106441-73-0
GENE NUMBER: GENBANK D11139 referred number; GENBANK D87258 referred number; GENBANK J04469 referred number; GENBANK J04599 referred number; GENBANK L06419 referred number; GENBANK L23808 referred number; GENBANK L26232 referred number; GENBANK M14058 referred number; GENBANK M28225 referred number; GENBANK M93221 referred number; GENBANK N74607 referred number; GENBANK U28014 referred number; GENBANK U46573 referred number; GENBANK U77735 referred number; GENBANK X15334 referred number; GENBANK X81832 referred number; GENBANK X92997 referred number; GENBANK Y14690 referred number; GENBANK AA100961 referred number; GENBANK AF004230 referred number; GENBANK AF022797 referred number; GENBANK AF052124 referred number; GENBANK AF055376 referred number; GENBANK AJ000342 referred number; GENBANK AL049946 referred number; GENBANK AY029208 referred number

L5 ANSWER 11 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2002347958 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12091409
TITLE: Microarray analysis of corneal fibroblast gene expression after interleukin-1 treatment.
AUTHOR: Mahajan Vinit B; Wei Cui; McDonnell Peter J 3rd
CORPORATE SOURCE: Department of Microbiology and Molecular Genetics, University of California-Irvine, Irvine, CA 92697, USA.
SOURCE: Investigative ophthalmology & visual science, (2002 Jul) 43 (7) 2143-51.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020702
Last Updated on STN: 20020716
Entered Medline: 20020715

ABSTRACT:
PURPOSE: To identify changes in gene expression in human corneal fibroblasts after exposure to interleukin-1alpha. METHODS: RNA was isolated from cultured human corneal fibroblasts after treatment with interleukin-1alpha and subjected to DNA microarray analysis. Changes in gene expression were determined by comparison with untreated cells in three independent experiments after a Bayesian statistical analysis of variance. RESULTS: Changes in gene expression were reproducibly observed in 165 genes representing previously identified and novel chemokines, matrix molecules, membrane receptors, angiogenic mediators, and transcription factors that correlated with pathophysiological responses to inflammation. Dramatic increases in gene expression were observed with exodus-1 (CCL20), **MMP-12**, and RhoA. CONCLUSIONS: DNA microarray analysis of the corneal fibroblast response to interleukin-1alpha provides important insight into modeling changes in gene expression and suggests novel therapeutic targets for the control of corneal inflammation.

CONTROLLED TERM:
Cells, Cultured
Computational Biology: MT, methods
*Cornea: DE, drug effects
Cornea: ME, metabolism
*Eye Proteins: GE, genetics
Eye Proteins: ME, metabolism
*Fibroblasts: DE, drug effects
Fibroblasts: ME, metabolism
*Gene Expression: PH, physiology
Gene Expression Profiling
Humans
*Interleukin-1: PD, pharmacology
Oligonucleotide Array Sequence Analysis
RNA: IP, isolation & purification
Research Support, Non-U.S. Gov't

CAS REGISTRY NO.: 63231-63-0 (RNA)
CHEMICAL NAME: 0 (Eye Proteins); 0 (Interleukin-1)

L5 ANSWER 12 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2002499097 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12235077
TITLE: Upregulation of matrix metalloproteinases in a model of T cell mediated tissue injury in the gut: analysis by gene array and in situ hybridisation.
AUTHOR: Salmela M T; MacDonald T T; Black D; Irvine B; Zhuma T; Saarialho-Kere U; Pender S L F
CORPORATE SOURCE: Department of Dermatology, Helsinki University Central Hospital, Helsinki, Finland.
SOURCE: Gut, (2002 Oct) 51 (4) 540-7.
Journal code: 2985108R. ISSN: 0017-5749.
PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20021004
Last Updated on STN: 20021213
Entered Medline: 20021107

ABSTRACT:
BACKGROUND AND AIM: Matrix metalloproteinases (MMPs) have been implicated in tissue remodelling and ulceration in inflammatory bowel disease and coeliac disease. Studies to date have concluded that stromelysin 1 is functionally involved in mucosal degradation. However, there are many other MMPs whose function in the gut is currently unknown. This work had two aims: firstly, to use gene array technology to measure changes in MMP and tissue inhibitor of metalloproteinase (TIMP) expression in a model of T cell mediated injury in the gut, and secondly, to correlate data from gene arrays with that generated by in situ hybridisation. METHODS: T cells in explants of human fetal gut were activated with pokeweed mitogen or anti-CD3 plus interleukin 12. Gene array analysis and in situ hybridisation were performed to investigate changes in MMP gene expression. RESULTS: Both gene array analysis and in situ hybridisation indicated marked upregulation of stromelysin 2 and macrophage ***metalloelastase*** expression in the explants associated with mucosal destruction. The arrays also confirmed our previous observation that interstitial collagenase (MMP-1), stromelysin 1 (MMP-3), and gelatinase B (MMP-9) are upregulated but there was no change in MMP-2, -7, -8, -9, -11, -13, -14-17, or -19. Following T cell activation, transcripts for TIMPs were reduced. CONCLUSIONS: These results show that there is differential upregulation of MMPs during T cell responses in the gut and suggest that further studies on the role of stromelysin 2 and macrophage ***metalloelastase*** may show that they have a functional role. In addition, the increase in MMPs and reduction in TIMPs suggest that the protease/antiprotease balance in the mucosa may determine the extent of mucosal degradation.

CONTROLLED TERM:
Collagenases: GE, genetics
Humans
In Situ Hybridization
*Intestine, Small: EN, enzymology
Matrilysin: GE, genetics
Matrilysin: ME, metabolism
Matrix Metalloproteinases: GE, genetics
*Matrix Metalloproteinases: ME, metabolism
Metalloendopeptidases: GE, genetics
Metalloendopeptidases: ME, metabolism
Oligonucleotide Array Sequence Analysis
RNA: AN, analysis
Research Support, Non-U.S. Gov't
*T-Lymphocytes: IM, immunology
Tissue Inhibitor of Metalloproteinase-1: GE, genetics
Tissue Inhibitor of Metalloproteinase-3: IM, immunology
Tissue Inhibitor of Metalloproteinases: GE, genetics
*Tissue Inhibitor of Metalloproteinases: ME, metabolism
*Up-Regulation

CAS REGISTRY NO.: 63231-63-0 (RNA)
CHEMICAL NAME: 0 (Tissue Inhibitor of Metalloproteinase-1); 0 (Tissue Inhibitor of Metalloproteinase-3); 0 (Tissue Inhibitor of Metalloproteinases); EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.- (Collagenases); EC 3.4.24.- (Matrix Metalloproteinases); EC 3.4.24.- (alveolar **macrophage elastase**); EC 3.4.24.- (collagenase 3); EC 3.4.24.- (membrane-type matrix metalloproteinase); EC 3.4.24.22 (stromelysin 2); EC 3.4.24.23 (Matrilysin)

L5 ANSWER 13 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2002209396 EMBASE
TITLE: Matrix metalloproteinases: Promoters of tumor progression and invasiveness.
AUTHOR: Sela B.-A.
CORPORATE SOURCE: Dr. B.-A. Sela, Institute of Chemical Pathology, Sheba Medical Center, Tel Hashomer 52621, Israel. benamis@sheba.health.gov.il
SOURCE: Israel Medical Association Journal, (2002) Vol. 4, No. 4, pp. 280-282.
Refs: 30
ISSN: 1565-1088 CODEN: IMAJCX
COUNTRY: Israel
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
030 Pharmacology
029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 20020708
Last Updated on STN: 20020708
CONTROLLED TERM: Medical Descriptors:
*cancer growth
*cancer invasion
human
clinical trial
nonhuman
metastasis
angiogenesis
protein degradation
in vivo study
enzyme activity
breast cancer: DT, drug therapy
colorectal cancer: DT, drug therapy
prostate cancer: DT, drug therapy
skin cancer
ovary cancer
bladder cancer
thyroid cancer: DI, diagnosis
thyroid papillary carcinoma: DI, diagnosis
enzyme activation
protein expression
cancer diagnosis
cancer cell
enzyme inhibition
drug mechanism
phage display
adenovirus vector
editorial
Drug Descriptors:
*matrix metalloproteinase: EC, endogenous compound
tumor promoter: EC, endogenous compound
tissue inhibitor of metalloproteinase: EC, endogenous compound
gelatinase A: EC, endogenous compound
matrilysin: EC, endogenous compound
gelatinase B: EC, endogenous compound
proteoglycan: EC, endogenous compound
tissue inhibitor of metalloproteinase 2: EC, endogenous compound
messenger RNA: EC, endogenous compound
tissue inhibitor of metalloproteinase 1: EC, endogenous

compound
macrophage elastase: EC, endogenous compound
angiostatin: EC, endogenous compound
matrix metalloproteinase inhibitor: CT, clinical trial
matrix metalloproteinase inhibitor: PD, pharmacology
matrix metalloproteinase inhibitor: DT, drug therapy
bb 3103: CT, clinical trial
bb 3103: PD, pharmacology
chelating agent: CT, clinical trial
chelating agent: PD, pharmacology
pyrimidine 2,4,6 trione: PD, pharmacology
decapeptide: PD, pharmacology
antisense oligonucleotide: PD, pharmacology
furin: EC, endogenous compound
stromelysin 3: EC, endogenous compound
stromelysin: EC, endogenous compound
interleukin 1beta: EC, endogenous compound
trypsin inhibitor: PD, pharmacology
unclassified drug

CAS REGISTRY NO.: (tissue inhibitor of metalloproteinase) 97837-28-0; (gelatinase A) 146480-35-5; (matrilysin) 141256-52-2; (gelatinase B) 146480-36-6; (tissue inhibitor of metalloproteinase 2) 124861-55-8; (tissue inhibitor of metalloproteinase 1) 140208-24-8; (angiostatin) 172642-30-7, 86090-08-6; (stromelysin 3) 145267-01-2; (stromelysin) 79955-99-0; (trypsin inhibitor) 9035-81-8
CHEMICAL NAME: Bb 3103
COMPANY NAME: Hoffmann La Roche

L5 ANSWER 14 OF 17 MEDLINE on STN
ACCESSION NUMBER: 2002161865 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11893658
TITLE: Roger S. Mitchell lecture. Uses of expression microarrays in studies of pulmonary fibrosis, asthma, acute lung injury, and emphysema.
AUTHOR: Sheppard Dean
CORPORATE SOURCE: Lung Biology Center, Center for Occupational and Environmental Health, Cardiovascular Research Institute, Department of Medicine, University of California, San Francisco, San Francisco, CA 94143, USA.. deans@itsa.ucsf.edu
SOURCE: Chest, (2002 Mar) 121 (3 Suppl) 21S-25S. Journal code: 0231335. ISSN: 0012-3692.
PUB. COUNTRY: United States
DOCUMENT TYPE: (LECTURES)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020315
Last Updated on STN: 20020418
Entered Medline: 20020417

ABSTRACT:
Expression microarrays are a powerful tool that could provide new information about the molecular pathways regulating common lung diseases. To exemplify how this tool can be useful, selected examples of informative experiments are reviewed. In studies relevant to asthma, the cytokine interleukin-13 has been shown to produce many of the phenotypic features of this disease, but the cellular targets in the airways and the molecular pathways activated are largely unknown. We have used microarrays to begin to dissect the different transcriptional responses of primary lung cells to this cytokine. In experiments designed to identify global transcriptional programs responsible for regulating lung inflammation and pulmonary fibrosis, we performed microarray experiments on lung tissue from wild-type mice and mice lacking a

member of the integrin family know to be involved in activation of latent transforming growth factor (TGF)-beta. In addition to identifying distinct cluster of genes involved in each of these processes, these studies led to the identification of novel pathways by which TGF-beta can regulate acute lung injury and emphysema. Together, these examples demonstrate how careful application and thorough analysis of expression microarrays can facilitate the discovery of novel molecular targets for intervening in common lung diseases.

CONTROLLED TERM: Check Tags: In Vitro
Animals
*Antigens, Neoplasm
*Asthma: GE, genetics
Gene Expression
*Genes, Regulator
Genetic Predisposition to Disease
Humans
Integrins: GE, genetics
Interleukin-13: PH, physiology
Lung: CY, cytology
Lung: ME, metabolism
Lung: PA, pathology
Matrilysin: GE, genetics
Metalloendopeptidases: GE, genetics
Mice
Mice, Knockout
***Oligonucleotide Array Sequence Analysis**
*Pulmonary Emphysema: GE, genetics
*Pulmonary Fibrosis: GE, genetics
Pulmonary Fibrosis: PA, pathology
*Respiratory Distress Syndrome, Adult: GE, genetics
Trans-Activation (Genetics)
Transforming Growth Factor beta: GE, genetics

CHEMICAL NAME: 0 (Antigens, Neoplasm); 0 (Integrins); 0 (Interleukin-13); 0 (Transforming Growth Factor beta); 0 (integrin alphavbeta6); EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.- (alveolar **macrophage elastase**); EC 3.4.24.23 (Matrilysin)

L5 ANSWER 15 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001261021 EMBASE

TITLE: [Analysis of gene expression with microarrays - Application in medicine].
BADANIE EKSPRESJI GENOW METODA MICROARRAY - PERSPEKTYWY WYKORZYSTANIA W MEDYCYNIE.

AUTHOR: Pawliczak R.; Kowalski M.L.

CORPORATE SOURCE: R. Pawliczak, Kat. Zaklad Immunol. Klin. AM Lodzi, ul. Pomorska 251, 92-213 Lodz, Poland

SOURCE: Alergia Astma Immunologia, (2001) Vol. 6, No. 2, pp. 77-85.
Refs: 28
ISSN: 1427-3101 CODEN: AAIMFF

COUNTRY: Poland

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 022 Human Genetics
027 Biophysics, Bioengineering and Medical Instrumentation

LANGUAGE: Polish

SUMMARY LANGUAGE: English; Polish

ENTRY DATE: Entered STN: 20010815
Last Updated on STN: 20010815

ABSTRACT: Microarrays are one of the latest breakthroughs in experimental molecular biology, which allow monitoring of gene expression for tens of thousands of genes in parallel and are already producing huge amounts of valuable data. Microarray RNA expression on a genome-wide scale is now a

proven technology, although the idea of analysis of expression many genes in one sample is not new. The development of clone printing technology and ***oligonucleotide*** synthesis allowed to produce high-density microarray. These systems together with more powerful and fast computer and software systems were applied not only in basic science but also in clinical medicine and pharmaceutical industry. In this publication the authors provide the information about the technology, available detection systems and data analysis software. Comprehensive review of current and fundamental papers using microarray technology application in rheumatoid arthritis, oncology, cystic fibrosis research, and allergic airways inflammation is also included.

CONTROLLED TERM: Medical Descriptors:
*DNA microarray
gene expression
analytic method
molecular cloning
nucleotide metabolism
computer system
computer program
clinical medicine
drug industry
data analysis
reverse transcription polymerase chain reaction
review
Drug Descriptors:
complementary RNA
gelatinase A
granulocyte colony stimulating factor
macrophage elastase
oligonucleotide
STAT protein
stromelysin
tissue inhibitor of metalloproteinase

CAS REGISTRY NO.: (gelatinase A) 146480-35-5; (stromelysin) 79955-99-0; (tissue inhibitor of metalloproteinase) 97837-28-0

L5 ANSWER 16 OF 17 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 4

ACCESSION NUMBER: 1998095538 EMBASE

TITLE: Overview of matrix metalloproteinase expression in cultured human cells.

AUTHOR: Giambernardi T.A.; Grant G.M.; Taylor G.P.; Hay R.J.; Maher V.M.; McCormick J.J.; Klebe R.J.

CORPORATE SOURCE: T.A. Giambernardi, Dept Cellular and Structural Biology, Univ of Texas Health Science Center, San Antonio, TX, United States

SOURCE: Matrix Biology, (1998) Vol. 16, No. 8, pp. 483-496.
Refs: 88
ISSN: 0945-053X CODEN: MTBOEC

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
021 Developmental Biology and Teratology
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 19980409
Last Updated on STN: 19980409

ABSTRACT: The matrix metalloproteinases (MMP) have been implicated in tumor invasion and metastasis both by immunohistochemical studies and from the observation that specific metalloproteinase inhibitors block tumor invasion and metastasis. **Oligonucleotide** primers for thirteen MMPs (MMP-1, MMP-2, MMP-3, MMP-7, MMP-8, MMP-9, MMP-10, MMP-11, **MMP-12**, MMP-13,

MMP-14, MMP-15, MMP-16) were optimized for use in RT-PCR. A semi-quantitative RT-PCR assay was used to determine the pattern of MMP mRNA expression in 84 normal and transformed or carcinogen transformed human cell lines and strains derived from different tissues. The results demonstrate one or more cell lines which express thirteen members of the MMP family. In addition, various oncogene transfected human fibroblast cell strains were analyzed for MMP expression. We confirm that over-expression of the H-ras oncoprotein correlates with up-regulation of MMP-9 and demonstrate that over-expression of v-sis also up-regulates MMP-9. A cell line immortalized following myc expression was found to up-regulate MMP-7, MMP-11 and MMP-13. Inappropriate expression of several MMP mRNAs was detected in breast, prostate, bone, colon and oral tumor derived cell lines. Identification of at least one cell line expressing each of thirteen MMPs and the observation of oncogene induced expression of several MMPs should facilitate analysis of the transcriptional mechanisms controlling each MMP.

CONTROLLED TERM: Medical Descriptors:
protein expression
oligonucleotide probe
reverse transcription polymerase chain reaction
cell transformation
oncogene
genetic transfection
fibroblast
gene overexpression
oncogene h ras
cell immortalization
tumor cell: ET, etiology
breast tumor: ET, etiology
prostate tumor: ET, etiology
bone tumor: ET, etiology
colon tumor: ET, etiology
mouth tumor: ET, etiology
human
controlled study
human cell
article
priority journal
Drug Descriptors:
*matrix metalloproteinase: EC, endogenous compound
messenger rna: EC, endogenous compound
carcinogen
collagenase: EC, endogenous compound
gelatinase a: EC, endogenous compound
stromelysin: EC, endogenous compound
matrilysin: EC, endogenous compound
neutrophil collagenase: EC, endogenous compound
gelatinase b: EC, endogenous compound
stromelysin 2: EC, endogenous compound
CAS REGISTRY NO.: (collagenase) 9001-12-1; (gelatinase a) 146480-35-5; (stromelysin) 79955-99-0; (matrilysin) 141256-52-2; (gelatinase b) 146480-36-6

L5 ANSWER 17 OF 17 MEDLINE on STN
ACCESSION NUMBER: 96275569 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8686751
TITLE: Expression of most matrix metalloproteinase family members in breast cancer represents a tumor-induced host response.
AUTHOR: Heppner K J; Matrisian L M; Jensen R A; Rodgers W H
CORPORATE SOURCE: Department of Cell Biology, Vanderbilt University, Nashville, Tennessee, USA.
CONTRACT NUMBER: R01 CA50468 (NCI)
R01 HD30472 (NICHD)

RO3 CA54942 (NCI)
+

SOURCE: American journal of pathology, (1996 Jul) 149 (1) 273-82.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960828
Last Updated on STN: 20000303
Entered Medline: 19960821

ABSTRACT:
Matrix metalloproteinase (MMP) family members have been associated with advanced-stage cancer and contribute to tumor progression, invasion, and metastasis as determined by inhibitor studies. In situ hybridization was performed to analyze the expression and localization of all known MMPs in a series of human breast cancer biopsy specimens. Most MMPs were localized to tumor stroma, and all MMPs had very distinct expression patterns. Matrilysin was expressed by morphologically normal epithelial ducts within tumors and in tissue from reduction mammoplasties, and by epithelial-derived tumor cells. Many family members, including stromelysin-3, gelatinase A, MT-MMP, interstitial collagenase, and stromelysin-1 were localized to fibroblasts of tumor stroma of invasive cancers but in quite distinct, and generally widespread, patterns. Gelatinase B, collagenase-3, and **metalloelastase** expression were more focal; gelatinase B was primarily localized to endothelial cells, collagenase-3 to isolated tumor cells, and **metalloelastase** to cytokeratin-negative, macrophage-like cells. The MMP inhibitor, TIMP-1, was expressed in both stromal and tumor components in most tumors, and neither stromelysin-2 nor neutrophil collagenase were detected in any of the tumors. These results indicate that there is very tight and complex regulation in the expression of MMP family members in breast cancer that generally represents a host response to the tumor and emphasize the need to further evaluate differential functions for MMP family members in breast tumor progression.

CONTROLLED TERM: Check Tags: Female
Antisense Elements (Genetics)
*Breast Neoplasms: CH, chemistry
Breast Neoplasms: PP, physiopathology
Carcinoma in Situ: CH, chemistry
Carcinoma in Situ: PP, physiopathology
Carcinoma, Ductal, Breast: CH, chemistry
Carcinoma, Ductal, Breast: PP, physiopathology
Endothelium: CH, chemistry
Epithelium: CH, chemistry
Fibroblasts: CH, chemistry
Humans
In Situ Hybridization
*Metalloendopeptidases: AN, analysis
Metalloendopeptidases: GE, genetics
RNA, Messenger: AN, analysis
Research Support, U.S. Gov't, Non-P.H.S.
Research Support, U.S. Gov't, P.H.S.
CHEMICAL NAME: 0 (**Antisense** Elements (Genetics)); 0 (RNA, Messenger); EC 3.4.24 (Metalloendopeptidases)

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